**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Patent Application No. 10/530,552

Applicant: JEONG et al.

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Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
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**DECLARATION UNDER 37 C.F.R. § 1.132 FROM LAK SHIN JEONG, PH.D.**

I, Lak Shin Jeong, hereby declare that:

1. I obtained a Ph.D. degree in 1992 in Medicinal Chemistry from the University of Georgia in Athens, GA. From 1993 to 1995, I was a Research Fellow at the National Cancer Institute, NIH. I have been with Ehwa Womans University, Seoul, Korea, since 1995, and presently, I am Assistant Dean, College of Pharmacy of the University. My areas of expertise include development of antiviral and antitumor nucleosides, computer aided drug design, and development of adenosine receptor ligands.

2. I am a named co-inventor in the above-identified application, and am familiar with the application and the pending claims. The Office Action has rejected claims for 12-15 and 26-42 under 35 USC §112, first paragraph, for an alleged non-enablement. The Office Action contends that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

3. Claims have been amended to recite a method of treating breast cancer. Based on tests conducted under my supervision or direction, as discussed below, the invention of such claims is fully enabled.

4. Tests were carried out in accordance with the guidelines established by the USPHS. Female nude BALB/cAn-NCrjBgi-nu mice (Orient, Seoul, Republic of Korea) were used at 7 to 8 weeks of age and maintained in the specific pathogen-free laboratory animal facility at Hanyang University (Seoul, Republic of Korea). A xenograft was established by subcutaneous injection of *in vitro* cultured tumor cells T47D ($3 \times 10^6$ cells/200 μL) or SK-BR-3 ($4 \times 10^6$ cells/150 μL) into the flank of mice. For xenograft with T47D cells, mice were supplemented with estradiol pellets (0.72 mg, released over 60 days; Innovative Research of America, Sarasota, FL). Tumors were measured in two diameters with calibers to permit calculation of tumor volume, $V = \{(D + d) / 2\}^3$, where $D$ and $d$ were the larger and smaller diameters, respectively. For drug treatment in mice, a stock solution of 0.5 mg/mL of drug was prepared by sonication in water. Five to seven days after injection, when the tumor width reached 1 to 3 mm, 20 animals were randomly selected, grouped, and treated with the indicated doses of LJ-529 ((2S,3S,4R,5R)-5-[2-chloro-6-(3-iodobenzylamino)purin-9-yl]-3,4-dihydroxytetrahydrothiophene-2-carboxylic acid methyl amide) daily and orally for 28 days. Each group contained five mice. The first day of drug treatment was set as day 0 and the tumor size and body weight were measured twice a week up to day 28.

5. Tumor growth was clearly suppressed in the LJ-529-treated group compared with the vehicle-treated group as examined by Student's $t$ test ($P < 0.05$ at indicated time points; see Fig. 1 attached to this Declaration). When one-way ANOVA was done to examine the group differences between tumor growth rates of T47D xenografts, statistical significance was seen between the groups [$F(3, 10) = 11.536$, $P = 0.001$]. Upon *post hoc* test using Scheffe, significant differences between vehicle- and all three LJ-529-treated groups were revealed (the mean differences were significant at the 0.05 level), but not within the drug-treated groups. The average tumor sizes are shown in Table 1. The results show that LJ-529 inhibits breast cancer growth in xenograft models.

Table 1. The effect of LJ-529 in a xenograft model of breast cancer in nude mice

| Cell line | Treatment | Day 0 | Day 7 | Day 14 | Day 21 | Day 28 |
|---|---|---|---|---|---|---|
| T47D | Control | 3.4 ± 0.2 | 15.1 ± 3.5 | 38.1 ± 4.0 | 10.1 ± 13.0 | 135.4 ± 15.1 |
| | Low | 3.7 ± 0.3 | 7.1 ± 2.4 | 20.1 ± 7.3 | 39.5 ± 21.1 | 53.9 ± 21.3 |
| | Medium | 3.5 ± 0.3 | 4.8 ± 0.1 | 9.1 ± 2.6 | 21.6 ± 4.7 | 25.9 ± 10.3 |
| | High | 2.3 ± 0.3 | 2.6 ± 0.4 | 9.8 ± 2.7 | 12.9 ± 0.5 | 19.8 ± 3.6 |
| SK-BR-3 | Control | 22.6 ± 8.1 | 23.0 ± 8.0 | 32.1 ± 10.8 | 34.1 ± 10.4 | 34.8 ± 10.3 |
| | Low | 19.9 ± 7.9 | 20.6 ± 7.7 | 22.8 ± 8.3 | 16.2 ± 6.6 | 7.6 ± 3.1 |
| | Medium | 16.3 ± 5.2 | 17.3 ± 5.1 | 18.0 ± 5.7 | 11.8 ± 3.7 | 5.6 ± 1.8 |
| | High | 16.4 ± 4.6 | 18.9 ± 4.6 | 19.5 ± 5.2 | 12.8 ± 3.4 | 6.1 ± 1.6 |

NOTE: Control, low, medium, and high groups were treated daily with vehicle (water), 50 μg/kg LJ-529, and 5 mg/kg LJ-529, respectively. The tumor volumes ($mm^3$) were presented as average ± SE.

6. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 5/8/06

Lak Shin Jeong, Ph.D.

Attachment - Fig. 1

Figure 1